

Systematic Review on Vitamin D Level in Apparently Healthy Indian Population and Analysis of Its Associated Factors

Sandhiya Selvarajan, Vikneswaran Gunaseelan, Nishanthi Anandabaskar, Alphienes Stanley Xavier, Sureshkumar Srinivasamurthy¹,
Sadish Kumar Kamalanathan², Jaya Prakash Sahoo²

Department of Clinical Pharmacology, JIPMER, Puducherry, ¹Department of Pharmacology, Karuna Medical College, Palakkad, Kerala, ²Department of Endocrinology, JIPMER, Puducherry, India

Abstract

Background: Vitamin D which is involved in the maintenance of bone mineral homeostasis has been found to portray various pleiotropic effects. Although it has been widely accepted that serum 25-hydroxy Vitamin D level above 30 ng/ml is considered optimal for the biological actions of Vitamin D, there is a need to explore the levels of Vitamin D reported among Indians from various regions of the country. Hence, this systematic review aims to appraise the status of Vitamin D levels reported from apparently healthy Indians across various parts of India. **Methodology:** A comprehensive literature search was carried out to identify the range of Vitamin D levels among apparently healthy individuals from various parts of India, with the search term “Vitamin D and India” in the search portals of PubMed, Google Scholar, Indmed, and ScienceDirect. A total of 2998 articles were retrieved by the above search strategy, of which only forty studies fulfilled the criteria to be included in the systematic review. Studies done in various states were compiled under the respective zones based on the classification of Indian zones as specified in Zonal maps of India. **Results:** The level of Vitamin D from all the forty included studies ranged from 3.15 ± 1.4 to 52.9 ± 33.7 ng/ml. The effect size of Vitamin D level was higher in the South Zone compared to other zones. **Conclusion:** The present study shows that Vitamin D deficiency is prevalent among apparently healthy Indians living in different regions of India, irrespective of their exposure to sunlight.

Keywords: Indians, supplementation, Vitamin D

INTRODUCTION

Vitamin D, a prohormone, is synthesized primarily by the photolysis of 7-dehydrocholesterol present in human skin by ultraviolet B radiation of wavelength 290–320 nm from sunlight [Figure 1]. Cod-liver oil, meat, egg, milk products, and mushrooms contribute toward dietary sources of Vitamin D in a meager quantity.^[1] Apart from playing a vital role in the maintenance of bone mineral homeostasis, Vitamin D has been found to portray pleiotropic effects as an anti-inflammatory, antiapoptotic, and antifibrotic agent. Further, it has been shown to play a major role in the regulation of cardiac, renal, and immune functions. Vitamin D deficiency has been found to be associated with increased risk for occurrence of diseases such as diabetes, schizophrenia, and malignancies.^[2-6]

Vitamin D status of an individual is assessed by the level of serum 25-hydroxy (25-OH) Vitamin D, one of the major circulating metabolites of Vitamin D. According to a study

done by Hollis to evaluate the biological effects of Vitamin D on calcium homeostasis, serum 25-OH Vitamin D level above 32 ng/ml is required for maintenance of bone health.^[7] Correspondingly, another study by Heaney has found that maximum calcium absorption in the gut is achieved above 30 ng/ml of serum 25-OH Vitamin D.^[8] These findings suggest to serum 25-OH Vitamin D level above 30 ng/ml as optimal for the biological actions of Vitamin D in an individual.

Currently, Vitamin D status is categorized based on Endocrine society guidelines as deficiency, insufficiency, and sufficiency based on serum 25-OH Vitamin D levels below

Address for correspondence: Dr. Sandhiya Selvarajan,
Department of Clinical Pharmacology, JIPMER, Puducherry, India.
E-mail: sandhiyaselvarajan@gmail.com

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20 ng/ml (50 nmol/L), 21–29 ng/ml (52.5–72.5 nmol/L), and 30–100 ng/ml (75–250 nmol/L), respectively.^[9] Although this classification is accepted widely, extensive efforts are being taken to interpret the basis of this criteria as most of the global populations are found to be Vitamin D deficient.^[10]

A recently conducted systematic review to appraise Vitamin D level from population across the continents found that nearly one-third of the studies from all over the world had Vitamin D level <20 ng/ml (50 nmol/L).^[11] Surprisingly, in spite of being a country of abundant sunshine, the prevalence of Vitamin D deficiency in India has been found to be nearly 70%–90% across all age groups.^[12–15] The average level of serum 25-OH Vitamin D level among Indians is strikingly lesser than the recommended criteria of 20 ng/ml as per the studies reported from various parts of India.^[16–18] One of the reasons for this could be that the normal reference range for Vitamin D level in Indians may be less than the criteria suggested. With the gaining momentum on the significance of Vitamin D level in promoting health, there is a need to explore the levels of 25-OH Vitamin D reported among Indians from various regions of the country. Hence, this systematic review aims to appraise the status of Vitamin D levels reported from apparently healthy Indians across various parts of India.

METHODOLOGY

A comprehensive literature search was carried out to identify the range of Vitamin D levels among apparently healthy individuals from various parts of India, with the search term “Vitamin D and India” in the search portals of PubMed, Google Scholar, IndMed, and ScienceDirect. All original research articles of community or hospital-based research done on Vitamin D levels of apparently healthy Indians published till June 30, 2015, were included in this study. From the retrieved articles, studies done among patients, pediatric age group, pregnant women, and lactating mothers were excluded from the study. Similarly, studies carried out on Indians living in foreign countries, case reports, *in-vitro* and animal studies were also excluded from the study. A total

of 2998 articles were retrieved by the above search strategy of which only forty studies fulfilled the criteria to be included in the systematic review [Figure 2]. Studies done in various states were compiled under the respective zones based on the classification of Indian zones as specified in Zonal maps of India [Table 1].^[19]

RESULTS

A total of forty studies from all over India including North, East, West, and South Zones with a sample size of 19761 were analyzed. In all the forty studies, the criteria for Vitamin D deficiency were kept below 20 ng/ml. The age group of the participants from the studies included in the review ranged from 13 ± 3.1 to 65.8 ± 7.5 years. Among the various zones, North followed by South contributed majority of the studies. Out of forty studies, 24 studies were from North followed by nine studies from South Zone with less number of studies from East and West. Applying the criteria of our search strategy, we did not come across studies from North East and Central Zones [Table 2].

The level of Vitamin D from all the forty included studies ranged from 3.15 ± 1.4 to 52.9 ± 33.7 ng/ml. The effect size of Vitamin D level was higher in the South Zone compared to other zones which were in almost in the same range of 12.3–14 ng/ml [Table 3]. Out of 40 studies included in the review, 14 (35%) studies had 25-OH Vitamin D level more than 20 ng/ml, of which one of the studies conducted in Chandigarh had Vitamin D level above 30 ng/ml. Majority of the North zone studies were from New Delhi followed by Lucknow and Chandigarh. Out of 24 studies done from North Zone, 22 studies had measured Vitamin D level using radioimmunoassay (RIA) while one study had used immunoassay the other one had used chemiluminescence assay. All the studies conducted from East Zone were only from Kolkata. The studies conducted from West Zone were from Mumbai and Pune. All the four studies from East Zone and three studies from West Zone had measured Vitamin D level using chemiluminescence and RIA methods, respectively. The South Zone studies were from Hyderabad, Tirupati, Vellore, and Nellore. Out of the ten studies done from South, seven studies had used RIA, two had used high-performance liquid chromatography, and one had

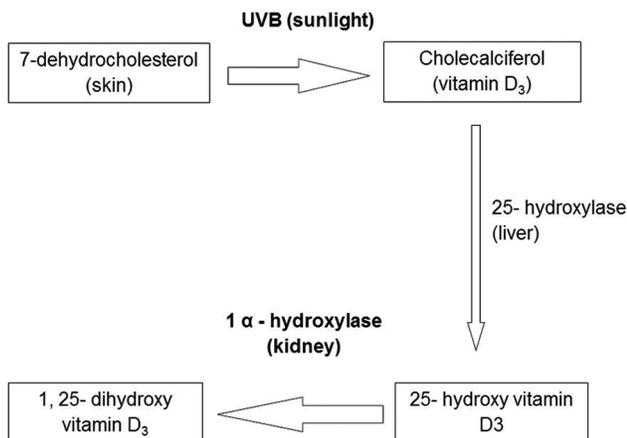


Figure 1: Vitamin D biosynthesis from sunlight

Table 1: Various zones of India and the states included under them

Zones	States included
North	Jammu and Kashmir, Himachal Pradesh, Punjab, Uttarakhand, Uttar Pradesh, Haryana
East	Bihar, Orissa, Jharkhand, and West Bengal
West	Rajasthan , Gujarat, Goa and Maharashtra
South	Andhra Pradesh, Telangana, Karnataka, Kerala and Tamil Nadu
Central	Madhya Pradesh and Chhattisgarh
North East	Assam, Sikkim, Nagaland, Meghalaya, Manipur, Mizoram, Tripura and Arunachal Pradesh

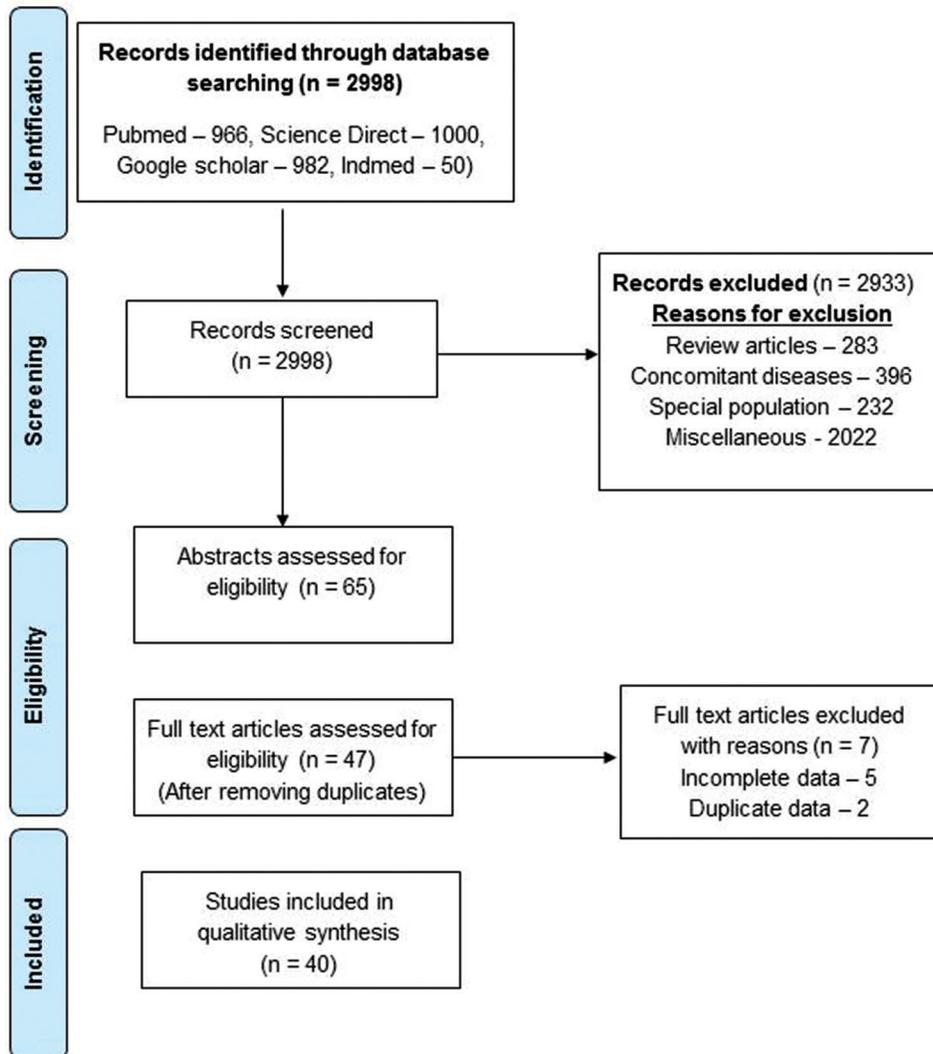


Figure 2: Flowchart describing the selection of studies for the systematic review

used chemiluminescence to measure Vitamin D levels. One of the forty studies had samples taken from representatives of North, East, West, South, and Central zones and they had used RIA for the analysis of Vitamin D level [Table 2].

In random effect model, the effect size of Vitamin D level was found to be higher in males compared to females as shown in Table 4. Similarly, the effect size of Vitamin D was found to be higher among middle-aged people compared to that of adolescents and those above 50 years of age. Those with normal body mass index (BMI) had a higher Vitamin D level compared to the population with higher BMI. People from rural areas had a higher Vitamin D level compared to those from urban areas. Vitamin D level was found to be higher during summer compared to that in winter [Table 4]. However, Vitamin D values except for summer and normal BMI were in the deficiency range of below 20 ng/ml. However, all these subgroups showed a larger difference in Vitamin D level in fixed-effect model compared to that of random-effect model [Figures 3 and 4].

DISCUSSION

India, a nation of abundant sunshine, is surprisingly found to have massive burden of Vitamin D deficiency among the public irrespective of their locality.^[13,14,20] Hence, we conducted a systematic review with the aim of evaluating the status of Vitamin D levels among apparently healthy population from various zones of India. Our study has shown the overall effect size of serum 25-OH Vitamin D level among Indians as 14.16 ng/ml (confidence interval [CI]: 13.27–15.05). This finding is similar to serum 25-OH Vitamin D concentration (14.35 ± 10.62 ng/ml [mean \pm standard deviation [SD]]) in a study conducted on apparently healthy middle-aged health-care professionals from various parts of India.^[15] This review found a difference in the overall effect size of Vitamin D level among South Indians is (17.45 [15.74–19.16] ng/ml) compared to Indians from other parts of India which varied between 12.3 and 14 ng/ml. This could be attributed to more sunny weather in South India compared to other parts of India.

Table 2: Baseline characteristics of apparently healthy individuals from various Vitamin D related studies done in India

Zone and Author	Age (years)	Sample Size (N)	Vitamin D (ng/ml) (Mean±SD)	Calcium (mg/dl)	Phosphate (mg/dl)	Parathormone (ng/ml)	Body mass index (Kg/m ²)	Assay
North Zone								
Bhatt <i>et al.</i> , 2014 (Delhi) ^[16]	40.2±7.9	137	18.9±6.7	-	-	-	-	RIA
Malhotra <i>et al.</i> , 2009 (Lucknow) ^[20]	26±6.32	50	4.5±3.4	-	-	-	-	RIA
Vupputuri <i>et al.</i> , 2006 (New Delhi) ^[21]	43.3±9.7	105	9.8±6	-	-	-	-	RIA
Goswami <i>et al.</i> , 2000 (New Delhi) ^[22]								
Soldiers-Winter	25±5	31	18.86±4.69	9.4, 0.68				RIA
Physicians and nurses-Winter	23±5	19	3.15±1.4	8.68, 0.4				
Depigmented-Winter	43±16	15	7.28±1.4	8.88, 0.4				
Physicians and nurses - Summer	24±4	19	7.19±3.19	9, 1.2				
Pregnancy - Summer	23±3	29	8.76±4.29	7.68, 1.08				
Goswami <i>et al.</i> , 2008 (New Delhi) ^[23]	>40	57	3.19±1.4	-	-	38.8, 18.2		RIA
Marwaha <i>et al.</i> , 2011 (Delhi) ^[17]	>50	1346	9.79±7.61					RIA
Zargar <i>et al.</i> , 2007 (Kashmir) ^[24]								
Rural	28.15±4.9	50	12.84±12.4			20.2, 2.3	-	RIA
Urban		42	11.34±9.66				-	RIA
Khadgawat <i>et al.</i> , 2012 (New Delhi) ^[25]								
Both gender 6-17 years	13±3.1	62	8.5±4.2	-	-	-		
Marwaha <i>et al.</i> , 2005 (Delhi) ^[26]	10 to 18	760	11.8±4.2	9.4, 0.97	-	-		RIA
Upper socioeconomic status		330	13.7±0.4				21.0, 4.7	
Lower socioeconomic status		430	10.4±0.4				17.1, 2.9	
Sahu <i>et al.</i> , 2009 (Lucknow) ^[27]								RIA
Females	10 to 20	121	13.32±6.4	8.68, 0.88	4.52, 0.93			
Goswami <i>et al.</i> , 2009 (New Delhi) ^[28]	33.7, 13.5	642	7±4.08	10, 0.64	3.68, 0.62			RIA
Tandon <i>et al.</i> , 2003 (New Delhi) ^[29]								RIA
Men	22.7±2.8	40	18.4±5.3	9.4, 0.7	3.9, 0.5		21.0, 1.48	
Women	23.4±3.1	50	25.3±7.4	9.5, 0.3	4.7, 0.4		20.43, 2.37	
Agarwal <i>et al.</i> , 2013 (New Delhi) ^[30]								
Arm 1 Female	56.3±7.71	30	12.99±6.74	8.37, 0.69	3.76, 0.47		27.12, 4.42	RIA
Arm 2 Female	53.84±5.12	31	12.92±8.2	8.55, 0.60	3.77, 0.58		28.87, 6.33	
Arm 3 Female	54.19±7.09	31	14.38±11.07	8.54, 0.76	3.72, 0.46		28.34, 4.90	
Agarwal <i>et al.</i> , 2014 (New Delhi) ^[31]								RIA
Females	56.3±7.6	71	12.73±7.63		3.76, 0.51	-	27.78, 5.37	

Contd...

Table 2: Contd...

Zone and Author	Age (years)	Sample Size (N)	Vitamin D (ng/ml) (Mean±SD)	Calcium (mg/dl)	Phosphate (mg/dl)	Parathormone (ng/ml)	Body mass index (Kg/m ²)	Assay
North Zone								
Gupta <i>et al.</i> , 2014 (Chandigarh) ^[32]	57.9±9.7	70	26.2±14.5	9.2, 0.8	3.40, 0.62			Chemiluminescence
Garg <i>et al.</i> , 2014 (Pune) ^[33]								RIA
Male <50 years	36.1±9.1	559	9.8±6.5	9.7, 0.5	3.5, 0.05	41.1, 29.8	24.1, 4	
Male >50 years	65.8±7.5	365	8.9±6.5	9.7, 0.4	3.5, 0.05	60.4, 32.6	25.5, 4	
Female <50 years	31±8.6	788	7±4.2	9.7, 0.5	3.8, 0.05	49.1, 26.5	22.8, 4.1	
Female >50 years	64.5±7.4	635	9.1±7.1	9.7, 0.4	3.8, 0.08	59.7, 35.2	28, 4.9	
Tandon <i>et al.</i> , 2014 (Jammu and Kashmir) ^[34]								Immuno assay
Postmenopausal women	56.22*	312	26.86*	-	-	-	-	
Marwaha <i>et al.</i> , 2009 (New Delhi) ^[35]								RIA
21-40 years Male	-	473	13.64±6.32	9.72, 0.6	3.65, 0.53	31.71, 13.04	22.8	
Priyambada <i>et al.</i> , 2014 (Lucknow) ^[36]	35.2±6.2	30	7.1±5.4					RIA
Arya <i>et al.</i> , 2004 (Lucknow) ^[37]	34.2±6.7	92	12.3±10.9					RIA
Marwaha <i>et al.</i> , 2011 (Delhi) ^[17]								
Male: 50-60 years	58±10.3	493	9.7±6.8	9.5, 0.4	3.4, 0.4	61, 41.9	25.79, 4.02	RIA
Male: 60-70 years	-	139	9±5.4	9.7, 0.5	3.4, 0.5	52.4, 28.7	26.38, 4.64	
Male: >70 years	-	160	10.9±7.8	9.7, 0.4	3.3, 0.4	55.1, 28.1	25.12, 3.92	
Female: 50-60 years	57.3±8.5	515	9.8±7.9	9.6, 0.4	3.7, 0.4	61.1, 39.4	29.5, 5.1	
Female: 60-70 years	-	210	9.2±8.8	9.8, 0.5	3.7, 0.5	52.7, 40.6	28.1, 4.7	
Female: >70 years	-	83	11±8.7	9.9, 0.5	3.8, 0.4	52.7, 40.6	26.7, 4.7	
Ramakrishnan <i>et al.</i> , 2011 (Chandigarh) ^[38]								RIA
Summer	19.4±1.48	329	52.9±33.7	-	4.18, 0.8	-	22.09, 3.35	
Winter	19.4±1.43	237	31.8±21.1	-	4.18, 1.02	-	22.1, 3.6	
Nagpal <i>et al.</i> , 2008 (New Delhi) ^[39]								RIA
Middle aged apparently healthy obese male	45.0±9.2	36	12±5	9.2, 0.9	3.59, 0.58	38, 23	26, 3.46	
Supplement group	42.4±6.6	35	14.6±5.82	9.2, 0.6	3.59, 0.58	33, 14.7	26.7, 4.54	
Garg <i>et al.</i> , 2014 (Delhi) ^[40]								RIA
Adolescent	13.3±2.5	1829	8.3±5.2	9.9, 0.5	4.2, 0.5	56.5, 33.7	-	
East zone								
Baidya <i>et al.</i> , 2012 (Kolkata) ^[41]	52.2±10.91	40	13.02±4.77	-	-		-	Chemiluminescence
Dutta <i>et al.</i> , 2013 (Kolkata) ^[42]	39.4±9.7	28	21.7±8.56	-	-		24.3, 2.7	Chemiluminescence
Maisnam <i>et al.</i> , 2014 (Kolkata) ^[43]								Chemiluminescence
Normal BMI	46.75±2.02	24	24.7±7.49	9.4, 0.63	4.07, 0.42		21.9, 1.5	
High BMI	42.35±4.31	32	11.1±4.18	8.9, 0.43	4.1, 0.28		28.2, 2.65	

Contd...

Table 2: Contd...

Zone and Author	Age (years)	Sample Size (N)	Vitamin D (ng/ml) (Mean±SD)	Calcium (mg/dl)	Phosphate (mg/dl)	Parathormone (ng/ml)	Body mass index (Kg/m ²)	Assay
East zone								
Basu <i>et al.</i> , 2015 (Kolkata) ^[44]						-		Chemiluminescence
Age 12-16 total	-	36	10, 8-17**	-	-			
Male	-	23	13, 10-17**	-	-			
Female	-	13	9, 4-23**	-	-			
Adult	58±9.5	1346	9.8±7.6	9.7, 0.5	3.6, 0.5	58.2, 38.7		
West Zone								
Kadam <i>et al.</i> , 2010 (Pune) ^[45]								RIA
Premenopausal women	45.6±4.8	80	9.6±4.4	-	-	34.28, 19.6		
Post-menopausal women	-	92	10.8±6.8		-			
Multani <i>et al.</i> , 2010 (Mumbai) ^[46]								RIA
Male	26.87±1.60	174	12.8±7.94	9.29, 0.54	3.88, 0.36		23.41, 3.4	
Female	26.33±1.58	40	10.94±4.54	9.15, 0.63	3.92, 0.32		21.59, 3.41	
Shivane <i>et al.</i> , 2012 (Mumbai) ^[47]								RIA
Total	30.38±3.55	1137	17.4±9.1	9.54, 0.51	3.69, 0.6		22.76, 4.18	
Male	30.11±3.53	558	18.9±8.9	9.56, 0.51	3.69, 0.62		22.71, 3.91	
Female	30.52±3.57	579	15.8±9.1	9.53, 0.51	3.67, 0.61		22.85, 4.36	
South Zone								
Reddy <i>et al.</i> , 2009 (Hyderabad) ^[48]								RIA
Men NBMI	26.8±4.33	75	23.48±19.05	10, 1.2	4.33, 0.31	37.14, 32.90	23.2, 1.73	
Men HBMI	27.2±4.3	74	20.56±13.07	10, 0.8	4.64, 0.31	49.52, 49.12	28.8, 2.58	
Women NBMI	28.6±4.65	77	20.28±21.41	9.6, 0.8	4.33, 0.62	44.76, 41.77	22.5, 1.93	
Women HBMI	28.7±4.65	77	9.8±11.58	9.2, 1.2	4.33, 0.31	64.76, 50.10	29.1, 3.24	
Yasovanthi <i>et al.</i> , 2011 (Hyderabad) ^[49]								HPLC
Premenopausal	37.36±4.18	206	21.77±3.85	9.90, 0.47	3.52, 0.23	-	25.92, 3.79	
Premenopausal osteoporosis	39.51±4.23	180	11.15±3.14	9.10, 0.41	3.58, 0.33	-	23.61, 3.72	
Post-menopausal	55.73±4.39	257	12.85±1.91	9.29, 0.33	4.21, 0.29	-	25.46, 3.31	
Post-menopausal osteoporosis	57.74±6.33	247	8.87±2.74	9.33, 0.64	4.44, 1.80	-	24.07, 4.88	
Harinarayan, <i>et al.</i> 2007 (Tirupati) ^[13]						-	-	RIA
Urban Male	46±9.69	134	18.54±9.26	9.74, 0.69	3.50, 0.81	-	-	
Urban Female	-	807	15.5±8.52	9.68, 0.56	3.64, 0.85	-	-	
Rural Male	43±14.46	109	23.73±8.35	10.06, 0.62	2.84, 0.73	-	-	
Rural Female	-	96	19±8.72	9.98, 0.58	2.74, 0.68	-	-	
Harinarayan <i>et al.</i> , 2011 (Tirupati) ^[18]								RIA
Premenopausal women	37.42±5.33	55	15.7±10.23	9.80, 0.37	3.37, 0.59	-	-	
Postmenopausal women	53.29±8.40	136	17.7±10.96	9.88, 0.46	3.46, 0.46	-	-	
Paul <i>et al.</i> , 2008 (Vellore) ^[50]								RIA

Contd...

Table 2: Contd...

Zone and Author	Age (years)	Sample Size (N)	Vitamin D (ng/ml) (Mean±SD)	Calcium (mg/dl)	Phosphate (mg/dl)	Parathormone (ng/ml)	Body mass index (Kg/m ²)	Assay
South Zone								
Postmenopausal women >50 years	60.1±5	150	20.85±8.63	9.41, 0.47	3.94, 0.67	-	24.74, 4.35	
Harinarayan <i>et al.</i> , 2004 (Tirupati) ^[12]	-							RIA
Rural		407	21±9.28	10, 1.01	3, 0.81			
Urban		125	13.52±6.59	9.71, 0.67	3.28, 0.59			
Shetty <i>et al.</i> , 2014 (Vellore) ^[51]								Chemiluminescence
Male	58±11.8	252	20.4±8.3	8.82, 0.43	4.45, 0.25		23.3, 4.5	
Bachali <i>et al.</i> , 2013 (Nellore) ^[52]	45	50	23.89*	-	-	-	-	HPLC
Beloyartseva <i>et al.</i> , 2012 (All zones) ^[15]	42.71±6.8	2119	14.35±10.62	-	-	-	-	RIA

*Only mean value, **Median and interquartile value, HPLC: High Performance liquid chromatography, RIA: Radio immuno assay

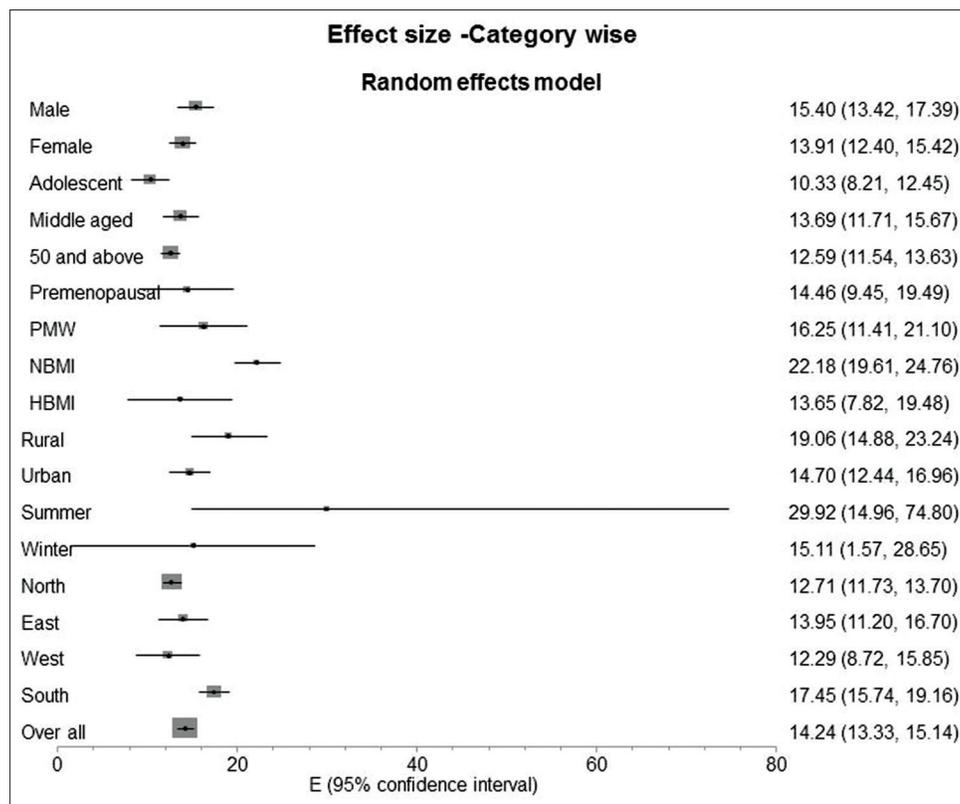


Figure 3: Effect size of Vitamin D using random-effects model

The review found that the mean effect size of serum 25-OH Vitamin D level is less in females (13.91, CI: 12.40–15.42) compared to males (15.40, CI: 13.42–17.39). This value is similar to a study done in healthy volunteers of Kashmir valley by Zargar *et al.* which showed that mean (SD) serum 25-OH Vitamin D level among females is 13.77 (11.05).^[24] Similarly, a study done among school children in New Delhi found boys having significantly higher 25-OH Vitamin D levels compared

to females ($P = 0.004$).^[26] Another study done to evaluate mean serum 25-OH Vitamin D values among adolescent boys and girls belonging to the same family near Lucknow, found that serum 25-OH Vitamin D in boys (67.5 ± 29.0 nmol/L) was higher than that in their sisters (31.3 ± 13.5 nmol/L, $P < 0.001$) during winter. This difference of Vitamin D level in adolescent girls compared to boys has been attributed to reduced exposure to sunlight, less nutrition as well as early

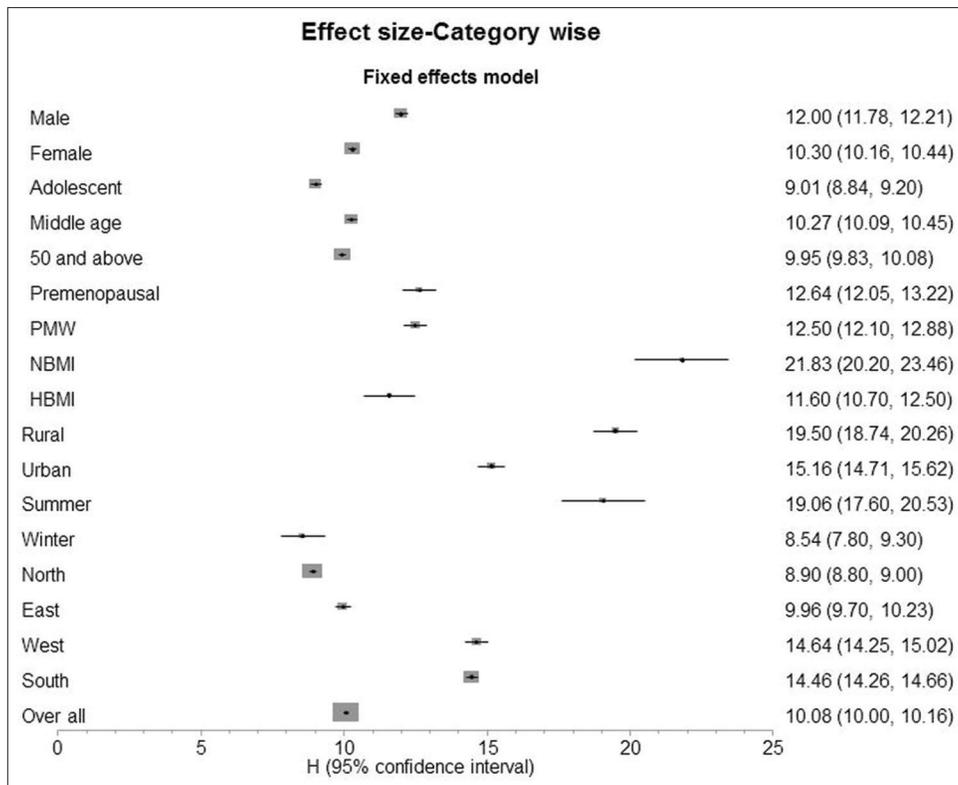


Figure 4: Effect size of Vitamin D using fixed-effects model

Table 3: Overall effect size of Vitamin D from various parts of India

Zones	No. of studies	Sample size	Effect size (ng/ml)	Confidence interval
North	24	11099	12.81	11.81-13.81
East	4	1506	13.95	11.20-16.69
West	3	1523	12.28	8.73-15.82
South	9	5633	17.45	15.74-19.16
All	40	19761	14.16	13.27-15.05

marriage and pregnancy among girls.^[27] Similarly, a study done by Ramakrishnan *et al.*, in urban college students from North India, found a significant difference of Vitamin D sufficiency in men (86.4%) compared to women (64.4%) ($P = 0.001$) in summer. However, this was attributed to the use of sunscreen among women students.^[38]

The review found middle-aged people to have higher Vitamin D level (13.69 [11.71–15.67] ng/ml) compared to adolescents (10.33 [8.21–12.45] ng/ml) and those aged above 50 years (12.59 [11.54–13.63] ng/ml). This finding was similar to the concentration of serum 25-(OH) Vitamin D (14.35 ± 10.62 ng/mL [mean ± SD]) from a study conducted in apparently healthy middle-aged health-care professionals from various parts of India.^[15] Likewise, a study done among people aged above 50 years in North India, has reported that nearly 91.2% of people in this age group are Vitamin D deficient with a mean 25-OH Vitamin D level of 9.72 ± 7.75 ng/ml and

a median value of 8.21 (0.18–100.0) ng/ml. The reason for a higher value in our study among those aged above 50 years could be a result of compiled Vitamin D level across the people from all regions of India.^[17] The finding of the review with respect to the value in adolescents is in concurrence to a study done among 760 apparently healthy school children of 10–18 years belonging to both lower and upper socioeconomic status in New Delhi, with an unadjusted mean serum 25-OH value of 11.8 ± 7.2 ng/ml. However in the same study, mean serum 25-OH value adjusted for lower ($n = 430$) and upper socioeconomic status ($n = 330$) was found to be 10.4 ± 0.4 and 13.7 ± 0.4 respectively ($P < 0.01$). The authors had concluded the reason for this significant difference among the children belonging to upper social strata could be attributed to their nutritional source of Vitamin D and calcium rich foods.^[26] On the contrary, a study done in college students from Chandigarh did not find association between socioeconomic status and Vitamin D level ($P = 0.55$).^[38] Likewise, another study done in 62 obese Asian Indian children and adolescent in the age group of 6–17 years found that all of them were Vitamin D deficient with a mean serum 25-(OH) Vitamin D level of 8.5 ± 4.2 ng/ml.^[25] These results illustrate that socioeconomic status, as well as nutritional status, does not alter Vitamin D level among the adolescents.

In our study, effect size of 25-OH Vitamin D level among postmenopausal women was found to be 16.25 ng/ml (CI: 11.41–21.1 ng/ml). This was similar to the level of Vitamin D (14.6 ± 7 ng/ml) as per the study done on

Table 4: Overall effect size of Vitamin D based on age, gender, BMI and socioeconomic status from various parts of India

Category	No. of studies	Sample size	Effect size random effect	Confidence interval	Effect size fixed effect	Confidence interval
Male	11	3334	15.40	13.42-17.39	12.0	11.78-12.21
Female	16	5969	13.91	12.40-15.42	10.30	10.16-10.44
Adolescent	5	2808	10.33	8.21-12.45	9.01	8.84-9.20
Middle age	17	3989	13.69	11.71-15.67	10.27	10.09-10.45
>50 years	11	6596	12.59	11.54-13.63	9.95	9.83-10.08
Pre-menopausal	3	521	14.46	9.45-19.49	12.64	12.05-13.22
Post-menopausal	5	1194	16.25	11.41-21.1	12.50	12.10-12.88
Normal BMI (Kg/m ²)	2	176	22.18	19.61-24.76	21.83	20.20-23.46
High BMI (Kg/m ²)	2	183	13.65	7.82-19.48	11.60	10.70-12.50
Rural	3	662	19.06	14.88-23.24	19.50	18.74-20.26
Urban	3	1108	14.70	12.44-16.96	15.16	14.71-15.62
Summer	2	348	29.92	-14.96-74.80	19.06	17.60-20.53
Winter	2	302	15.11	1.57-28.65	8.54	7.80-9.30

postmenopausal women of the age group of 50–67 years by Harinarayan.^[53] Our finding is also similar to a study done on postmenopausal women ($n = 150$) aged 50 years and above from Tamil Nadu, with mean 25-OH Vitamin D level of 20.85 (8.63) ng/ml.^[50] One of the major reasons quoted for reduced Vitamin D level in this group of population is reduced exposure to sunlight owing to more indoor confinement.

The study found a significant difference in Vitamin D level among people with normal BMI (22.18 [19.61–24.76] ng/ml) compared to those with high BMI (13.65 [7.82–19.48] ng/ml). Even nondiabetic obese urban Asian Indians with increased total abdominal fat were found to be associated with Vitamin D insufficiency.^[16] The inverse relationship between weight and Vitamin D level is attributed to unavailability of Vitamin D owing to its accumulation with in fat compartments in overweight people.^[54] Vitamin D level was found to be higher in rural population (19.06 [CI: 14.88–23.24] ng/ml) compared to urban population (CI: 14.70 [12.44–16.96] ng/ml). The decline in outdoor activity and effluence is considered to be a reason for Vitamin D deficiency among urban population.^[55] A study done in a village from North India found that 70% of rural population has Vitamin D deficiency with mean serum 25-OH Vitamin D level of 36.4 ± 22.5 nmol/L. This value was found to be higher than the mean 25-OH Vitamin D level of 13.5 ± 3.0 nmol/L among urban population. This difference was attributed to longer duration of exposure to sunlight in rural population.^[23] There was a significant variation in Vitamin D level measured among studies conducted during summer (29.92 [–14.96–74.80] ng/ml) compared to the studies done in winter (15.11 [1.57–28.65] ng/ml) [Table 4]. Following administration of Vitamin D supplementation in a study done on apparently healthy Indian women with Vitamin D deficiency, the increase in mean serum 25-OH Vitamin D level was found to be higher during summer compared to that of winter.^[20] Similarly, a study done in rural area of North India showed a significant difference ($P < 0.001$) in 25-OH Vitamin D level in girls and women during summer (55.5 ± 19.8 nmol/L, mean ± SD) compared to that of (winter 27.3 ± 12.3 nmol/L,

mean ± SD).^[27] Further, a study done in Chandigarh on college students showed the mean ± SD of 25-OH Vitamin D level during summer was 52.9 ± 33.7 ng/ml, with a median value of 48 ng/ml while the same in winter was 31.8 ± 21.1 ng/ml, with a median value of 30 ng/ml ($P < .001$). In the same study after excluding the subjects with features of healed rickets, the mean 25-OH Vitamin D level was found to be 55.0 ± 33.9 ng/ml and 31.8 ± 20.7 ng/ml at the end of summer as well as winter, respectively.^[38]

CONCLUSION

The present study shows that Vitamin D deficiency is prevalent among apparently healthy Indians living in different regions of India, irrespective of their exposure to sunlight as per the current Institute of Medicine (IOM) recommendation of normal Vitamin D level. The deficiency is commonly seen among the Indians regardless of age, gender, menopausal status, residing in rural, or urban areas.

The primary source of Vitamin D being sunlight, it was assumed for a long time that a country like India with ample sunshine exposure all through the year will be devoid of Vitamin D deficiency. Conversely, studies done in Indian population was found to be portraying a diverse scenario.^[13,14] One of the reasons for Vitamin D deficiency among Indians is ascribed to decreased synthesis of Vitamin D as a consequence of darker skin, use of sunscreen, indoor lifestyle, reduced intake of dietary products rich in Vitamin D, etc.^[32] Hence, it is being suggested that Vitamin D supplementation has to be used widely among Indians to treat Vitamin D deficiency. It is also suggested to create awareness among the population regarding the prevalence of Vitamin D deficiency and the measures to be taken to avoid it by increasing exposure to sunlight, intake of Vitamin D rich diet as well as Vitamin D supplementation if required. Suggestions are given regarding fortification of food with Vitamin D through national healthcare programs.^[56,57] However, before carrying out such programs, the effects of Vitamin D overdose resulting in hypercalcemia, calcium stones, metastatic calcification, etc.,

should be taken into consideration.^[57] Studies recommend that serum 25-OH Vitamin D levels should be interpreted along with serum PTH levels. This is because Vitamin D deficient subjects with normal PTH levels are found to exhibit either no or less adverse effects on bone health. A study done in adolescents and adults to evaluate the relationship between serum 25-OH Vitamin D, PTH, and bone mineral density in Indians has suggested that possibly the increased serum PTH level determines bone health irrespective of serum 25-OH Vitamin D.^[40] Recently, it has been reported that IOM reference values for Vitamin D normal level needs to be interpreted in an appropriate manner and Vitamin D deficiency need not be considered as a pandemic. It is also stated that unnecessary screening procedure, as well as Vitamin D supplementation, needs to be evaded.^[10] The continuing deliberations have raised the concerns regarding the normal cutoff value of Vitamin D level as well as the need for Vitamin D supplementation in Indian population. Further, studies are needed to establish the normal value for serum 25-OH Vitamin D level in Indian population.

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Conflicts of interest

There are no conflicts of interest.

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